Amendment and Response Applicant: Kenneth Kaushansky

Serial No.: 08/347,748 Filed: December 1, 1994

For METHODS FOR STIMULATING ERUTHROPOIESIS USING HEMATOPOIETIC PROTEINS

Amendments to the Claims

This listing of the claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-8 Canceled

- 9. (currently amended) A method for stimulating erythropoiesis comprising administering to a mammal in need thereof a composition comprising a mammalian thrombopoietin protein of at least 323 amino acid residues selected from the group consisting of:
- (a) a protein comprising the sequence of amino acids of SEQ ID NO: 4 from amino acid residue 45 to amino acid residue 379; and
- (b) a protein comprising a sequence of amino acids shown in SEQ ID NO: 2 from amino acid residue 1 to residue 353; and
- (c) a protein comprising the sequence of amino acids shown in SEQ ID NO: 2 from amino acid residue 22 to residue 353,
- species homologs of (a) wherein said thrombopoietin protein stimulates proliferation or differentiation of myeloid or lymphoid progenitors, in combination with a pharmaceutically acceptable vehicle in an amount sufficient to produce an increase in proliferation or differentiation of erythroid cells.
- $10.\,$ (original) The method of claim 9, wherein said mammal has a hemoglobin level of less than 11 gm/100 ml of blood.
- $11. \hspace{0.5cm}$ (original) The method of claim 9, wherein said mammal has a hematocrit of less than 30%.
- $12. \hspace{0.5cm} \mbox{(original)}$ The method of claim 9, wherein said mammal has a reticulocyte count of less 0.8%.
- (original) The method of claim 9, wherein said mammal has been treated with radiation or chemotherapy.

14. (Canceled)

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Cancel claim 15

- 16. (original) The method of claim 9, wherein 1.0×10^5 to 100×10^5 units TPO/kg/day is administered to said mammal.
- (original) The method of claim 9, wherein 1.2 lg/kg/day to 114 lg
 TPO/kg/day is administered to said mammal.
- 18. (currently amended) A method for stimulating erythropoiesis comprising administering to a mammal in need thereof <u>a composition comprising an erythropoietin protein and</u> a composition comprising a mammalian thrombopoietin protein of at least 323 amino acid residues selected from the group consisting of:
- (a) a protein comprising the sequence of amino acids of SEQ ID NO: 4 from amino acid residue 45 to amino acid residue 379; and
- (b) a protein comprising a sequence of amino acids shown in SEQ ID NO: 2 from amino acid residue 1 to residue 353; and
- (c) a protein comprising the sequence of amino acids shown in SEQ ID NO: 2 from amino acid residue 22 to residue 353,
- species homologs of (a) wherein said thrombopoietin protein stimulates proliferation or differentiation of myeloid or lymphoid progenitors, and erythropoietin, in combination with a pharmaceutically acceptable vehicle in an amount sufficient to produce an increase in proliferation or differentiation of erythroid cells.
- (original) The method of claim 18, wherein said mammal has a hemoglobin level of less than 11 gm/100 ml of blood.
- (original) The method of claim 18, wherein said mammal has a hematocrit of less than 30%.
- (original) The method of claim 18, wherein said mammal has a reticulocyte count of less than 0.8%.
- 22. (original) The method of claim 18, wherein said mammal has been treated with radiation or chemotherapy.

23. (Canceled)

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(original) The method of claim 18, wherein the EPO is human

Cancel claim 25.

- 26. (original) The method of claim 18, wherein 1.0×10^5 to 100×10^5 units TPO/kg/day and 1 to 150 units EPO/kg/day are administered to said mammal.
- (original) The method of claim 18, wherein 1.2 lg/kg/day to 114 lg
 TPO/kg/day and 1 to 150 units EPO/kg/day are administered to said mammal.
- 28. (currently amended) A method for stimulating erythropoiesis comprising administering to a patient in need thereof a composition comprising an erythropoietin protein and a composition comprising a mammalian thrombopoietin protein of at least 323 amino acid residues selected from the group consisting of:
- (a) a protein comprising the sequence of amino acids of SEQ ID NO: 4 from amino acid residue 45 to amino acid residue 379; and
- (b) a protein comprising a sequence of amino acids shown in SEQ ID NO: 2 from amino acid residue 1 to residue 353; and
- (c) a protein comprising the sequence of amino acids shown in SEQ ID NO: 2 from amino acid residue 22 to residue 353,
- species homologs of (a) wherein said thrombopoietin protein stimulates the proliferation or differentiation of myeloid or lymphoid progenitors, and erythropoietin, in combination with a pharmaceutically acceptable vehicle, in an amount sufficient for increasing reticulocyte counts at least 2-fold over baseline reticulocyte counts within fourteen days.
- 29. (currently amended) A method for stimulating erythropoiesis comprising administering to a patient in need thereof a composition comprising a mammalian thrombopoietin protein of at least 323 amino acid residues selected from the group consisting of:
- (a) a protein comprising the sequence of amino acids of SEQ ID NO: 4 from amino acid residue 45 to amino acid residue 379; and
- (b) a protein comprising a sequence of amino acids shown in SEQ ID NO: 2 from amino acid residue 1 to residue 353; and

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(c) a protein comprising the sequence of amino acids shown in SEQ ID NO: 2 from amino acid residue 22 to residue 353,

species-homologs of (a) wherein said thrombopoietin protein stimulates proliferation or differentiation of myeloid or lymphoid progenitors, in combination with a pharmaceutically acceptable vehicle, in an amount sufficient for increasing reticulocyte counts at least 2-fold over baseline reticulocyte counts within fourteen days.

- 30. (currently amended) A method for stimulating erythropoiesis comprising administering to a patient in need thereof a composition comprising a mammalian thrombopoietin protein of at least 323 amino acid residues selected from the group consisting of:
- (a) a protein comprising the sequence of amino acids of SEQ ID NO: 4 from amino acid residue 45 to amino acid residue 379; $\frac{1}{2}$ and
- (b) a protein comprising a sequence of amino acids shown in SEQ ID NO: 2 from amino acid residue 1 to residue 353; and
- (c) a protein comprising the sequence of amino acids shown in SEQ ID NO: 2 from amino acid residue 22 to residue 353, wherein said thrombopoietin protein proteins stimulates proliferation or differentiation of myeloid or lymphoid progenitors, and erythropoietin, in combination with a pharmaceutically acceptable vehicle in an amount sufficient for increasing reticulocyte counts at least 2-fold over baseline reticulocyte counts and platelet levels to at least 20,000/mm³ within fourteen days.
- 31. (currently amended) A method for stimulating erythropoiesis comprising administering to a mammal in need thereof a composition comprising a mammalian thrombopoietin protein of at least 323 amino acid residues selected from the group consisting of:
- (a) a protein comprising the sequence of amino acids of SEQ ID NO: 4 from amino acid residue 45 to amino acid residue 379; and
- (b) a protein comprising a sequence of amino acids shown in SEO ID NO: 2 from amino acid residue 1 to residue 353; and
- (c) a protein comprising the sequence of amino acids shown in SEQ ID NO: 2 from amino acid residue 22 to residue 353, wherein said thrombopoietin protein stimulates proliferation or differentiation of myeloid or lymphoid progenitors, in combination with a pharmaceutically acceptable vehicle in an amount sufficient for increasing reticulocyte counts at least 2-fold over baseline reticulocyte counts and platelet levels to at least 20,000/mm³ within fourteen days.—